UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/787,122	02/27/2004	Simon Benita	14945.0001	4640

7590 10/02/2007

D. Douglas Price
Steptoe & Johnson
BOX PTO
1330 Connecticut Avenue, NW
Washington, DC 20036

EXAMINER	
SASAN, ARADHANA	

ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
10/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/787,122	BENITA ET AL.	
	Examiner	Art Unit	
	Aradhana Sasan	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-2, 4-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 07/10/2007 are acknowledged.

2. Claim 3 was cancelled.

3. Claims 1-2 and 4-15 are included in the prosecution.

Response to Arguments

Objection to the Specification

4. Applicant's amendment of the specification to correct the typographical errors is acknowledged. The objection of 03/29/2007 is withdrawn.

Objections to claims 4 and 11

5. Applicant's amendments of claims 4 and 11 for informalities are acknowledged. The claim objections of 03/29/2007 are withdrawn.

Drawings

6. Applicant's amendment of including the heading "Brief Description of Drawings" is acknowledged.

Rejection of claim 1 under 35 USC § 112, first paragraph

7. Applicant's arguments with respect to the rejection of claim 1 under 35 USC § 112, first paragraph as not reasonably providing enablement for all compounds with free NH_2 groups and all antibodies have been fully considered and are persuasive. The rejection of 03/29/2007 is withdrawn.

Rejection of claims 14-15 under 35 USC § 112, second paragraph

8. Applicant's arguments and amendments with respect to the rejection of claims 14-15 under 35 USC § 112, second paragraph as being indefinite because of the phrase "with the other products necessary" have been fully considered and are persuasive. The rejection of 03/29/2007 is withdrawn.

Rejection of claims 1-2, 7-11 under 35 USC § 102(b)

9. Applicant's arguments with respect to the rejection of claims 1-2, 7-11 under 35 USC § 102(b) as being anticipated by Kadouche et al. (WO 01/52889) have been fully considered and are found persuasive. The rejection of 03/29/2007 is withdrawn.

Rejection of claims 3-6, 12-15 under 35 USC § 103(a)

10. Applicant's arguments with respect to the rejection of claims 3-6, 12-15 under 35 USC § 103(a) as being unpatentable Kadouche et al. (WO 01/52889), in view of Yang et al. (Drug Development Research, 2000), and further in view of Kirpotin et al. (Biochemistry, 1997) have been fully considered and are found persuasive. The rejection of 03/29/2007 is withdrawn.

11. After further consideration new rejections are made on the basis of newly found prior art.

NEW REJECTIONS/OBJECTIONS:

The following is a list of new rejections/objections:

Claim Objections

12. Claim 4 is objected to under 37 CFR 1.75(c) as being in improper form because it is dependent on claim 3, which was cancelled on 07/10/2007.

Claim Rejections - 35 USC § 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "said compound" in lines 4-5. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 1-2 and 4-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kadouche (WO 01/52889) in view of Singh et al. (Cancer Letters 84 (1994) 15-21).

(The corresponding US patent application publication (US 2002/0106324 A1 is being used as a reference since an English translation of the WIPO document (WO 01/52889) was not available).

The claimed invention is a cationic oil in water emulsion comprising a compound with free NH_2 groups and an antibody and a method for producing the emulsion. The compound is linked to the antibody by a heterobifunctional linker. The emulsion contains an active drug. The antibody (polyclonal or monoclonal) targets antigens.

Kadouche et al. (US 2002/0106324 A1) teaches a monoclonal antibody coupled to a liposome type vector or to cationic type emulsions and also a cationic lipid (Page 5, [0064]). Kadouche teaches native antibodies as immune effectors used in anti-tumoral therapies, which involves "blocking a receptor of the target cell or an anti-idiotypic vaccination for the tumoral antigen" (Page 2, [0018]). Also taught are polyclonal antibodies along with their affinity for ferritins (Page 3, [0047] and Page 4, Table 1). Kadouche teaches an anti-ferritin monoclonal antibody and specifically AMB8LK which was "used to carry out a sandwich ELISA test to detect human ferritins" (Page 7, [0114]).

Kadouche does not expressly teach cationic lipids selected from the group consisting of a C_{10}-C_{24} alkylamine, a C_{10}-C_{24} alkanolamine and a cholesterol ester and a heterobifunctional linker.

Singh teaches monensin liposomes linked to tumor specific monoclonal antibodies with full retention of immunoreactivity (Abstract). Dipalmitoyl phosphatidylcholine (DPPC), cholesterol (CHOL), and stearyl amine (SA) were used in the liposomal preparation (Page 16, left hand column, 2.1). "Immunotoxins against the CEA (anticarcinoembryonic antigen) were produced with these antibodies by conjugating the native ricin A chain to the antibody using the heterobifunctional reagent, *N*-succinimidyldithiopropionate (SPDP)" (Page 16, left hand column, 2.2). [^{3}H]Monensin liposomes were prepared with the lipid composition DPPC/CHOL/SA/PDP-SA (5:3:1:1) (Page 16, right hand column, 2.4). The heterobifunctional reagent SPDP was used to

introduce pyridyl disulphide groups into the monoclonal antibodies (Mabs) (Page 16, right hand column, 2.5).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a product with a monoclonal antibody coupled to a liposome type vector, a cationic type emulsion, or a cationic lipid, as suggested by Kadouche, combine it with the monensin liposomes linked to tumor specific monoclonal antibodies with full retention of immunoreactivity, as suggested by Singh, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Singh discloses that monoclonal antibody targeted monensin liposomes were 100 times more potent than monensin liposomes in potentiating the activity of ricin A immunotoxins against various tumor cell lines in vitro (Abstract).

Regarding instant claim 1, the limitations of a combination product comprising a positively charged oil in water emulsion, cationic lipid, antibody, and where the cationic lipid is linked to the antibody by a heterobifunctional linker would have been obvious to one skilled in the art over the teachings of Kadouche and Singh. Kadouche provides the teaching of coupling an antibody to a cationic type emulsion. Singh provides the teaching of a combination product comprising an active ingredient containing liposome linked to monoclonal antibodies using heterobifunctional reagents.

Regarding instant claim 2, the limitation of the product having a positive zeta charge would have been obvious to one skilled in the art over the cationic emulsion

taught by Kadouche. A positive zeta charge is an intrinsic feature of a cationic emulsion and would be obvious to one skilled in the art.

Regarding instant claim 4, the limitation of the cationic lipids stearylamine or oleylamine would have been obvious to one skilled in the art over the stearylamine taught by Singh.

Regarding instant claim 5, the limitation of the emulsion comprising colloid particles having an oily core surrounded by an interfacial film would have been obvious to one skilled in the art over the liposomal preparation that comprises the cationic lipid stearylamine taught by Singh. One skilled in the art would know that the charge on an emulsion is conferred by the charge of the lipids used. Therefore, the use of a cationic lipid would lead to a positively charged emulsion.

Regarding instant claim 6, the limitation of the active principle in the emulsion would have been obvious to one skilled in the art over the monensin liposomes taught by Singh.

Regarding instant claim 7, the limitation of the polyclonal antibody would have been obvious to one skilled in the art over the polyclonal antibodies taught by Kadouche.

Regarding instant claim 8, the limitations of the monoclonal antibody would have been obvious to one skilled in the art over the monoclonal antibodies taught by Singh.

Regarding instant claim 9, the limitation of the antibody targeting an antigen on the surface of a pathological cell would have been obvious to one skilled in the art over the tumor specific antibodies taught by Singh.

Regarding instant claims 10-11, the limitations of the antibody targeting H-ferritin and AMB8LK antibody would have been obvious to one skilled in the art over the anti-ferritin monoclonal antibody AMB8LK taught by Kadouche.

Regarding instant claim 12, the limitation of the linker would have been obvious to one skilled in the art over the heterobifunctional reagent SPDP taught by Singh.

Regarding instant claims 13-15, the limitations of a method for producing the combination product would have been obvious to one skilled in the art over the heterobifunctional reagent SPDP that was used to introduce pyridyl disulphide groups into the monoclonal antibodies, as taught by Singh, and by the coupling of monoclonal antibodies to a liposome type vector or a cationic emulsion, as taught by Kadouche.

Conclusion

17. Due to the new grounds of rejection, this action is made non-final.

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MICHAEL P. WOODWARD
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600